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RESEARCH ARTICLE

Case Series of Non-small Cell Lung Cancer Treated With Mountain Ginseng Pharmacopuncture

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Abstract
This study aims to observe the efficacy of mountain Ginseng (*Panax ginseng* C.A. Meyer) pharmacopuncture (MGP) on cancer patients using different delivery methods of acupoint injection and intravenous infusion. Six non-small cell lung cancer (NSCLC) patients who met the eligibility criteria were observed. Two patients were continuously infused with MGP (20 mL/day) intravenously, and the other two patients were injected with MGP (10 mL/day) on acupoint LU1 bi-lateral continuously. The remaining two patients received MGP therapy using both methods of delivery. Results were followed by computed tomography (CT) after every cycle; each cycle lasted for 28 days. Two patients infused intravenously showed stable disease and two patients injected on LU1 showed progressive disease. Two patients treated using both methods showed stable disease during the intravenous infusion period and progressive disease during the intraacupuncture injection period. One patient showed progressive disease in the latest chest CT in spite of receiving MGP intravenous infusion. We suggested that MGP may be more effective when used as an intravenous infusion rather than acupoint injection in NSCLC patients.

1. Introduction

Lung cancer is clinically divided into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). SCLC is neuroendocrine neoplasm with an aggressive biological behavior and generally a marked initial response to polychemotherapy. NSCLC is a heterogeneous group of neoplasm with various differentiation characteristics. NSCLC represents 75–80% of all primary lung cancers which make up the bulk of lung cancer cases [1,2].

At presentation, only about 30% of NSCLC are localized and surgery is usually the optimal treatment choice for the disease [3]. However, even in cases of successful surgeries, recurrences are observed in most patients as the disease takes its course. For inoperable patients with locally advanced disease or metastatic disease at the time of diagnosis, no curative treatments are available. Overall, the prognosis of lung cancer is poor, with a less than 15% of 5-year survival rate [4]. Generally accepted prognostic factors, such as TNM staging,

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performance status, and histological types do not serve as a reliable prediction source for disease progression in an individual patient [3–5].

In Korea, ginseng (*Panax ginseng* C.A. Meyer) has long been used as a general tonic or as an adaptogen to promote longevity and enhance bodily functions. It has also been claimed to be effective in stress reduction, fatigue, oxidants, diabetes mellitus and cancer [6]. Panax meaning "cure all" in Greek, it is widely accepted that wild ginseng is more effective than cultivated ginseng for anticancer and chemoprevention purposes [7,8].

Pharmacopuncture therapy (PT) is a therapeutic method derived from combining herbal medicine and acupuncture therapy [9]. Mountain Ginseng Pharmacopuncture (MGP) is a type of PT used in cancer treatments and other progressive disorders such as amyotropic lateral sclerosis [10]. Our team has conducted numerous researches during the past several years on MGP including anecdotal tales, case reports, toxicity studies, cell culture experiments, animal experiments, mechanism studies and some of case reports related with cancer patients [11–19]. However, these data of dosage, treatment period and cancer types are not sufficient to support the anticancer effect of MGP. Therefore this clinical study was conducted to observe the efficacy of MGP on NSCLC patients treated by different types of delivery methods.

2. Methods

2.1. Eligibility

A total of 6 NSCLC patients were observed from August 2007 to December 2009. Informed consents were obtained from all patients. The places of settings were made in two hospitals in Daejeon and Wonju, Korea. Eligibility is shown below:

(1) Histologically or radiologically diagnosed NSCLC;
(2) Eastern Cooperative Oncology Group (ECOG) ≤ 3;
(3) Measurable malignant disease using the international standard of Response Evaluation Criteria in Solid Tumors (RECIST); complete/partial response (CR/PR), progression/stable disease (PD/SD);
(4) Completion of anticancer drugs and/or radiation treatment 3 weeks prior to participation;
(5) Recovery from all side effects of anticancer drugs and/or radiation treatment;
(6) Proper bone marrow function (peripheral absolute granulocyte count $>150\times10^9$/L, platelet count $>100\times10^9$/L);
(7) Proper liver function (bilirubin $\leq$1.5 mg/dL, serum glutamic pyruvic transaminase or serum glutamic oxaloacetic transaminase $<3\times$normal) and kidney function (creatinine $\leq$1.5 mg/dL).

2.2. Treatment

Each patient received either MGP 20 mL/day of intravenous infusion or MGP 10 mL/day of acupoint (LU1) injection. There were 4 weeks (28 days) in one treatment cycle. MGP was prepared as the method of previous studies [18,19].

2.3. Tumor measurement for response rate

Computed tomography (CT) scan was performed at the beginning of the treatment to measure the initial tumor size, then again at every 2 treatment cycles (8 weeks). Response rate was measured by the RECIST standard; complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) was used. Compared to initial tumor size, a 30% or greater decrease in size was confirmed as PR, a 20% or greater increase was confirmed as PD; if neither PR nor PD was confirmed, then it is an SD.

3. Results

3.1. Patients characteristics

Of the 6 patients that were followed, there were five male (83.3%) and one female (16.7%) patients. They all had NSCLC, two squamous cell carcinoma (33.3%), two adenocarcinoma (33.3%) and others (33.3%). Three patients were in stage IV (50.0%) and two patients were in stages III (33.3%) (Table 1).

3.2. Case reports

Case 1 was a 64-year-old male patient diagnosed with NSCLC adenocarcinoma stage IV. He was initially diagnosed at a hospital in October 2006 and had gone through resection of right upper lobe and right lower lobe along with adjuvant chemotherapy. After chemotherapy, another cancer was found in left upper lobe (Figure 1A). LU1 acupoint injection of MGP 10 mL/day was administered from July to October 2008. The treatment outcome was unsuccessful and the tumors had progressed according to the chest CT (Figure 1B). Then the patient had changed to intravenous infusion of MGP 20 mL/day from October 2008 to February 2009. During the treatment, cancer markers in blood analysis showed normal range, and tumor growth has stopped for 9 weeks (Figure 1C). However, even with continuous MGP intravenous infusion, increasing masses were observed in February 2009 (Figure 1D).

Case 2 was a 60-year-old male patient diagnosed with NSCLC squamous cell carcinoma stage IV with

Table 1 Characteristics of patients

Case no.	1	2	3	4	5	6
Gender						
Male	❍	❍		❍	❍	❍
Female			❍			
NSCLC tumor history		❍	❍			
Adenocarcinoma						
Squamous cell carcinoma	❍					❍
Others				❍	❍	
Tumor stage	IV	IV	IV	NA	IIIA	IIIB
Pretreatment						
Chemotherapy	❍	❍				
Operation	❍	❍				
Method of MGP treatment						
Acupoint injection	❍			❍	❍	
Intravenous injection	❍	❍	❍			❍
Age (yr)	Median (range)			66.5 (60–78)		

MGP=mountain ginseng pharmacopuncture; NSCLC=non-small cell lung carcinoma; NA=not available.

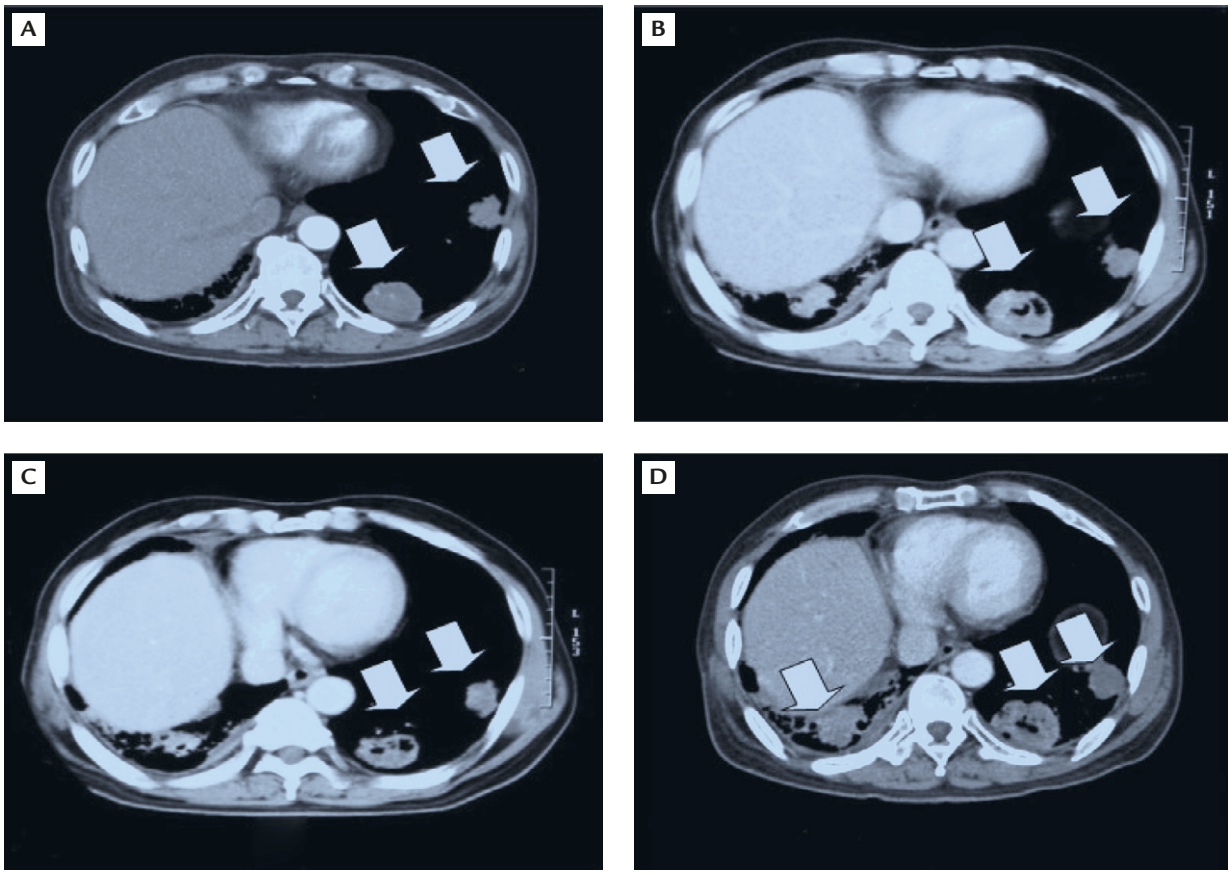

Figure 1 Chest computed tomography (CT) taken during treatment. (A) Chest CT on August 11th, 2008. (B) Chest CT on October 6th, 2008. (C) Chest CT on December 9th, 2008. (D) Chest CT on February 9th, 2009. The tumors in (B) were increased than the tumors in (A). The tumors in (C) showed no interval changes compared with the tumors in (B). The tumors in (D) were markedly increased than the tumors in (C).

metastasis to right anterior thoracic wall (Figure 2A). He was initially diagnosed at a hospital in December 2004 and had gone through multiple surgeries due to uncontrolled metastasis to right and left upper lobes (December 2004, April 2006, and August 2006). Nonetheless, the tumor has progressed and the patient received extensive chemotherapy from October 2007 to May 2008. We administered intravenous infusion of MGP 20 mL/day from November 2008 to February 2009. During treatment, tumor growth has shown stable condition for 4 weeks (Figure 2B) but chest CT taken on February 2009 has revealed slight progression of the disease (Figure 2C).

Case 3 was a 62-year-old female patient diagnosed with NSCLC squamous cell carcinoma stage IV (T4N2M1). Her primary tumor was located in right middle lobe with multiple metastasis to regional lymph nodes and bones (Figure 3A). She was initially diagnosed at a hospital in July 2008. She had refused all conventional therapy. We administered acupoint injection of MGP 10 mL/day from August to October 2008, but tumor was markedly increased accompanied by pleural effusion according to the chest CT taken in September 2009 (Figure 3B).

Case 4 was a 70-year-old male patient diagnosed with NSCLC. He was initially diagnosed at a hospital in July 2008 with masses found in RML (Figure 4A). He had breathing difficulties with weight loss. He refused all conventional therapies due to his old age and wished to be treated with oriental medicine. We administered acupoint injection of MGP 10 mL/day from July to August 2008, but tumor size has slightly increased according to the chest CT taken in August 2008 (Figure 4B).

Case 5 was a 65-year-old male patient diagnosed with NSCLC squamous cell carcinoma stage IIIa with masses located in left upper lobe (Figure 5A). He was initially diagnosed at a cancer center in November 2007 and had refused all conventional therapies. We administered intravenous infusion of MGP 20 mL/day from November 2007 to May 2008. The tumor growth has shown stable condition for 20 weeks (Figure 5B). However it was not continued the intravenous infusion delivery with his refusal and MGP treatment via acupoint injection 10 mL/day was applied from June to September 2008. During treatment, tumor size has slightly increased according to the chest CT taken in September 2008 (Figure 5C). While the patient was resting at home pneumonia was found with lung cancer (Figure 5D).

Case 6 was a 78-year-old male patient diagnosed with NSCLC squamous cell carcinoma stage IIIb. His primary tumor was located in right middle lobe (Figure 6A) with accompanying symptoms of dyspnea, hemoptysis, fever and weight loss. He was initially diagnosed at a hospital on August 2008 and

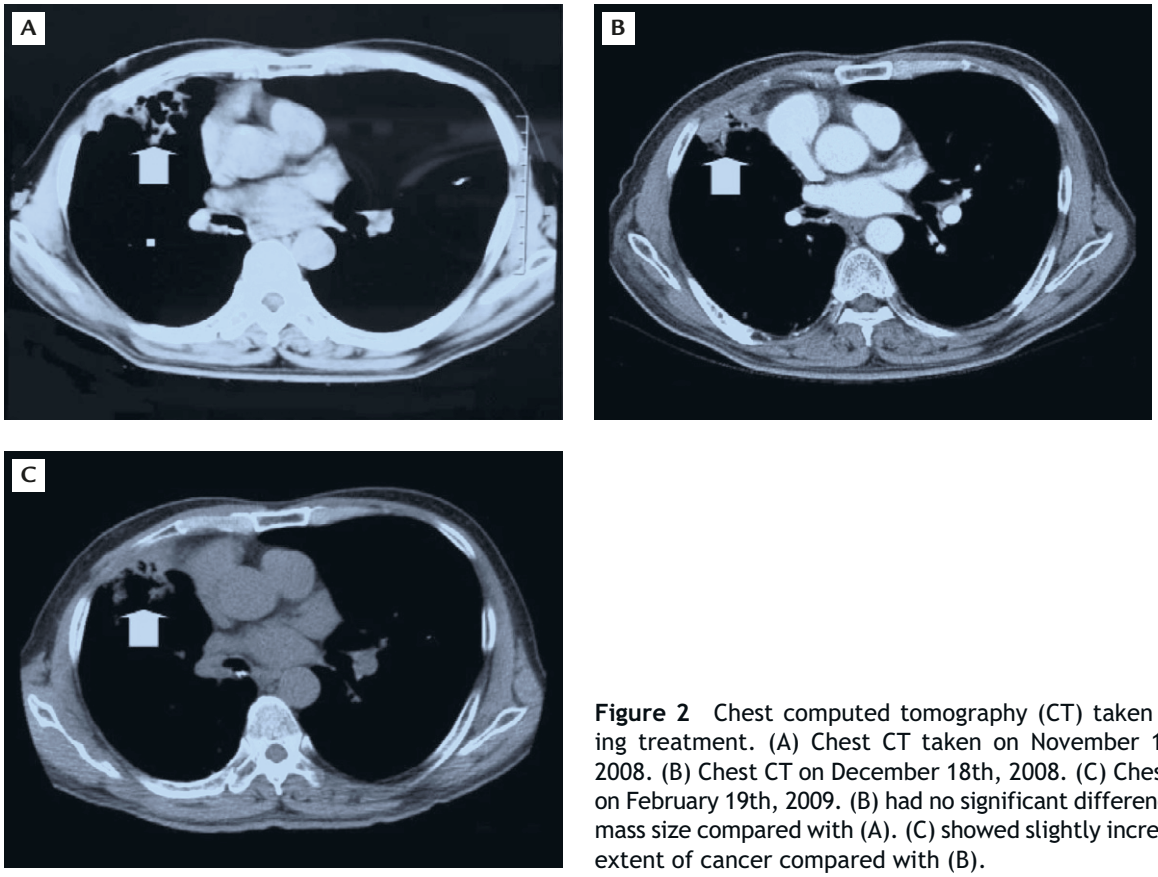

Figure 2 Chest computed tomography (CT) taken during treatment. (A) Chest CT taken on November 11th, 2008. (B) Chest CT on December 18th, 2008. (C) Chest CT on February 19th, 2009. (B) had no significant difference in mass size compared with (A). (C) showed slightly increased extent of cancer compared with (B).

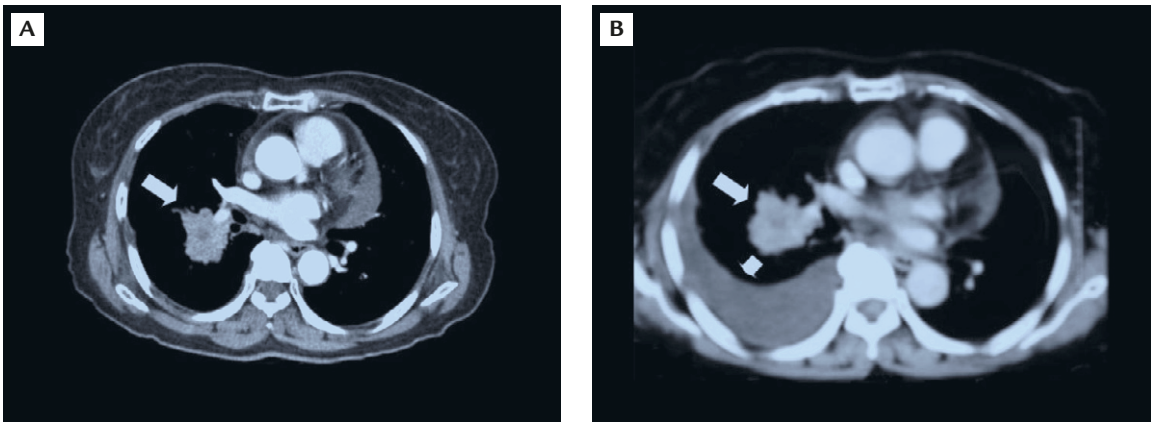

Figure 3 Chest computed tomography (CT) taken during treatment. (A) Chest CT taken on July 22nd, 2008. (B) Chest CT on September 3rd, 2008. (B) showed markedly increased right pleural effusion and both lung metastatic nodules than (A).

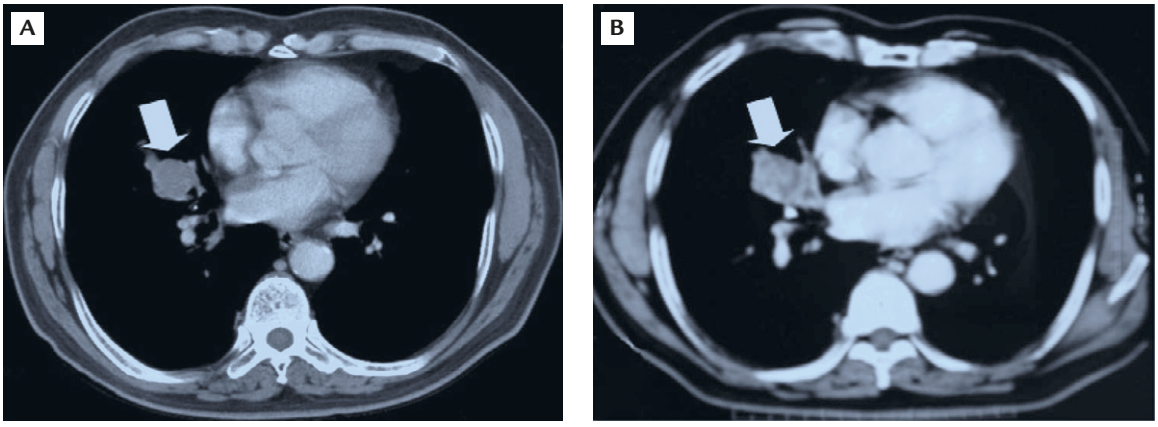

Figure 4 Chest computed tomography (CT) taken during treatment. (A) Chest CT on July 14th, 2008. (B) Chest CT on August 22nd, 2008. Both images showed known lung cancer mass about 3 cm in size in the right middle lobe. (B) showed slightly increased mass size than (A).

had refused all conventional therapies due to his old age. We administered intravenous infusion of MGP 20 mL/day from August 2008 to December 2009. During treatment, all cancer related symptoms and the tumor growth has shown stable condition for 16 months (Figure 6B). Patient was discharged later on as he refused all further treatments.

4. Discussion

In terms of incidence and mortality, lung cancer is one of the leading cancers in the world. The incidence of lung cancer is rapidly growing in Korea as well, now accounting for 12% of all cancers, with relatively low survival rate [20–22].

Treatment for lung cancer depends on their histological subtypes and staging of the disease. The strongest predictor of the treatment guidelines and prognosis for lung cancer is the American Joint Commission on Cancer (AJCC)'s staging system for NSCLC [23]. The TNM staging system is based on the pathological size of the primary tumor (T), regional lymph nodes involvement (N) and presence or absence of distant metastasis (M). Approximately 45% of lung cancers are limited to chest, where surgical resection is possible with postsurgery survival rate ranging from 55 to 85% [24,25]. Unfortunately, most NSCLC patients are diagnosed at locally advanced stages (stage IIIb) or metastatic stages (stage IV) and the survival time without treatment is poor (<6 months) [26–28]. Chemotherapy, such as gemcitabine, is the standard treatment for advanced NSCLC, but most NSCLC patients undergoing chemotherapy experience common side effects of these chemotherapeutic regiments including nausea/vomiting, nephrotoxicity, and neurotoxicity [29].

Today, cancer patients receiving conventional medical care also seek other treatments such as complementary and alternative medicine (CAM) [30]. CAM is more prevalent in Asia due to the popularity of traditional medicine. Oriental medicine is used by many countries on various diseases, and currently there are many clinical trials and researches being

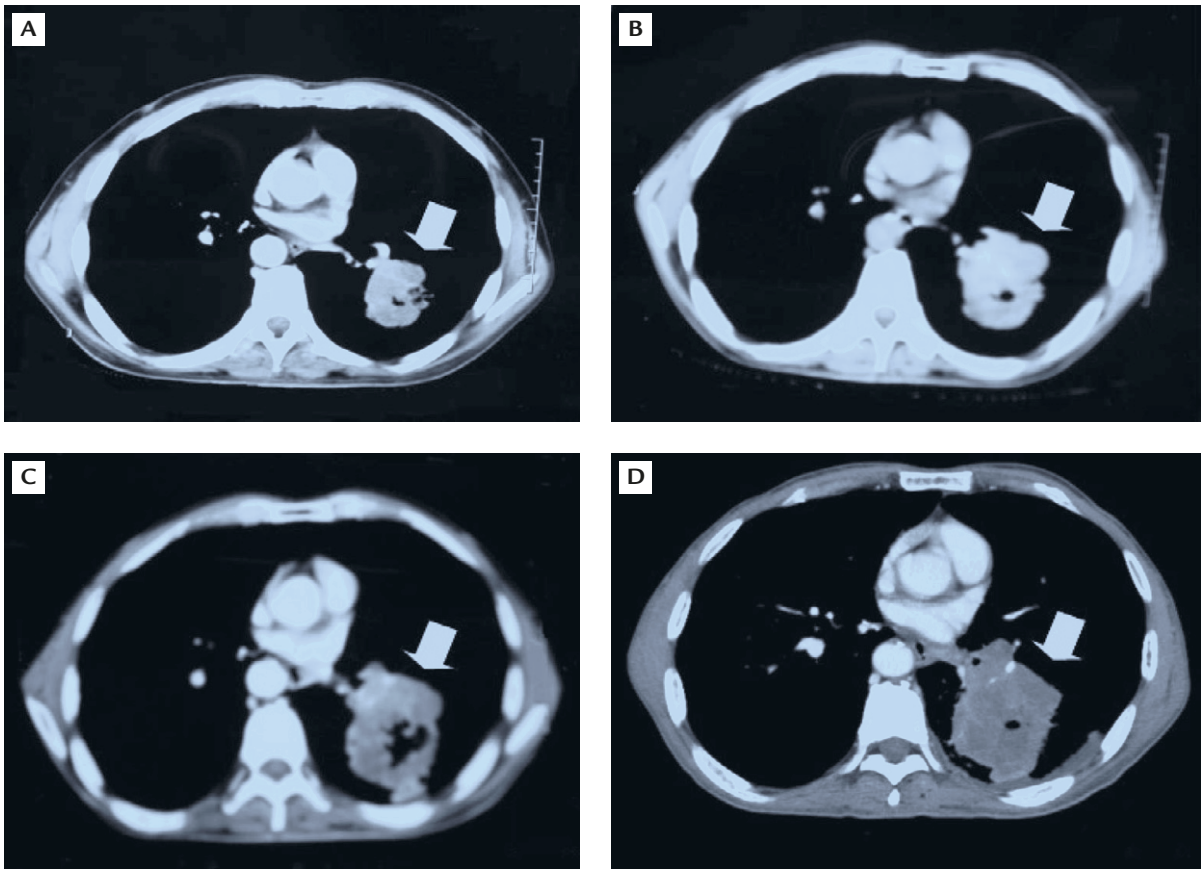

Figure 5 Chest computed tomography (CT) taken during treatment. (A) Chest CT on November 29th, 2007. (B) Chest CT on May 8th, 2008. (C) Chest CT on September 23rd, 2008. (D) Chest CT on November 27th, 2008. (A) and (B) were taken before and after the intravenous infusion of MGP and the tumors had shown no interval change. (B) and (C) were taken before and after the acupoint injections and the tumor had increased. (D) showed lung mass with pneumonia.

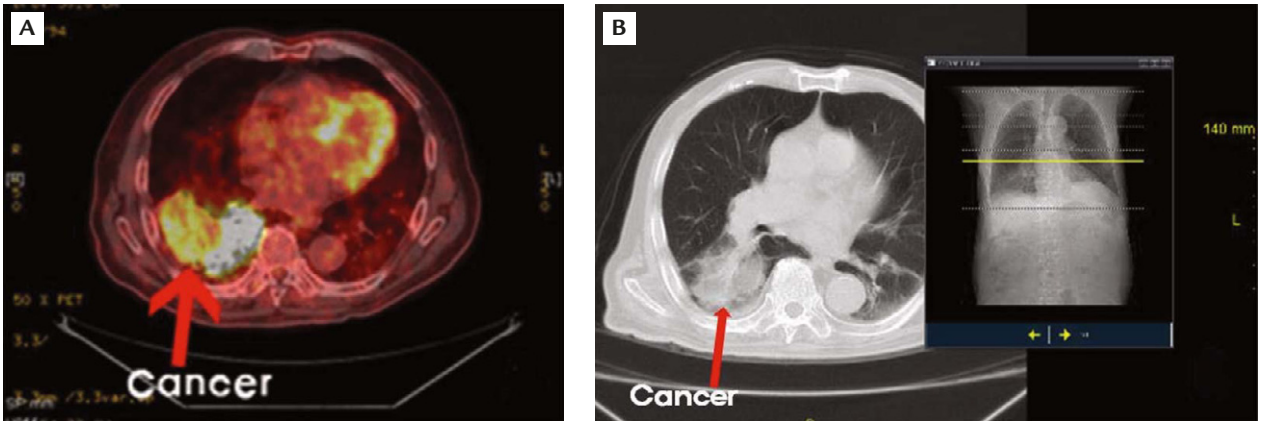

Figure 6 Positron emission tomography (PET) and chest computed tomography (CT) taken before and after the intravenous infusion of mountain Ginseng pharmacopunture and the tumors had shown no interval change. (A) PET and CT in August 2008. (B) Chest CT followed in October 2009.

done in the field of traditional medical oncology with the advancement of CAM worldwide.

Mountain Ginseng (Ginseng; *Panax ginseng* C.A. Meyer), a Korean traditional medicinal herb has been used clinically in Korea and also in other Asian countries for thousands of years [6]. In cancer care, most studies claim that the pharmacological effects of ginseng are attributed to its bioactive constituents such as ginsenosides, saponins, phytosterols, peptides, polysaccharides, fatty acids,

Table 2 Summary of patient cases

Case no.	Date of diagnosis	Prior given conventional therapy	Administration on mode of MGP	No. of cycles*	Results (RECIST)
1	10/2006	Operation Chemothrapy	Acupoint injection	2	Disease progression (PD)
			Intravenous infusion	4	No interval changed (SD)
2	12/2004	Operation Chemothrapy	Intravenous infusion	4	No interval changed (SD)
3	7/2008	None	Acupoint injection	2	Marked increased Right pleural effusion and both lung metastatic nodules (PD)
4	7/2008	None	Acupoint injection	1	Slightly increased mass size (SD)
5	11/2007	None	Acupoint injection	2	Increased mass size (PD)
			Intravenous infusion	5	No interval changed (SD)
6	7/2008	None	Intravenous infusion	16	No interval changed during 14 cycles (SD)

*One cycle consists of 28 days of being treated with MGP daily. MGP=mountain ginseng pharmacopuncture; RECIST=Response Evaluation Criteria in Solid Tomors; PD=progression disease; SD=stable disease.

polyacetylenes, vitamins, and minerals. There are many types of flavonoid compounds such as quercetin, hesperidin and anthocyacanidins. Several flavonoids scavenge reactive oxygen species. Other flavonoids suppress the pro-inflammatory and growth promoting gene mediated by nuclear factor kappa B (NF-κB). Flavonoids also interfere with signal transduction pathways, reducing tumor initiation and promotion [31].

In previous studies, MGP has demonstrated its anti-tumor effects and safety [11,12]. Inhibitory effect against hepatic metastasis using Colon 26-L5 carcinoma cells injected through hepatic portal vein was shown [8]. Induction of apoptosis on A549 human lung cell cancer lines was also observed [13]. Clinical studies using MGP on multiple metastatic hepatocellular carcinoma cases [15] and on other various cancers over stage III have been performed recently [19]. These researches show the potential of MGP as an effective measure in maintaining tumor size and enhancing the quality of life of cancer patients.

This study was done to observe the effectiveness of MGP on NSCLC patients depending on the delivery method. The patients were treated over one cycle of MGP from August 2007 to December 2009 at the hospitals in Daejeon and Wonju, Korea. Six patients were observed during and after the completion of treatment.

As seen in Table 2, patients who received MGP via acupoint injection at LU1 have not shown any improvements or remained stable, whereas most patients who received MGP via intravenous infusion showed stable disease for 2–16 cycles.

Although this study is an investigator initiated observational trial (I.I.T.) of a case series, it still holds significance as MGP treatments are already clinically used for cancer management in Korean oriental medicine. Though the amount used for intravenous infusion (20 mL/day) compared to intra acupoint injection (10 mL/day) could act as a bias, intravenous delivery method was linked to better prognosis of patients according to our observation. This research suggests the future application of intravenous delivery method could play an important factor in conducting pharmacopuncture treatment in Korea, where intravenous infusion uses are limited unlike China where Traditional Chinese Medicine frequently incorporates the intravenous delivery method for herbal injections.

In conclusion, confirmed efficacies of MGP for NSCLC cases are not yet clear, but the results of our study demonstrated the delivery of MGP via intravenous infusion with better efficacy than the acupoint injection. Further studies of MGP are needed to build more concrete evidence.

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